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Research Article

In-Vitro Fertilization Outcome in Patients with Polycystic Ovary Syndrome: Role of Age and Maternal Body Weight

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Abstract

Objective: to evaluate the impact of pre-gestational maternal age and body weight on the outcome of IVF in women with PCOS.

Design: a retrospective study on women with PCOS undergoing IVF.

Methods: Medical records of 200 known cases of polycystic ovary syndrome women treated in a third level referral center by the same therapeutic protocol were evaluated retrospectively. Demographic data, maternal body mass index, hormonal profile (LH, FSH, estradiol, anti-mullerian), IVF cycle parameters and outcome were documented. Patients were classified to three groups based on their body mass index (Normal: 18.5-24.9, overweight: 25-30, obese≥30). IVF cycle parameters and outcome were compared in these 3 groups. Effect of age was also evaluated by comparing the results in patients aged <35 and ≥35.

Results: Mean age of patients was 32.5 (±5.2). 72 patients had normal BMI, 85 patients were overweighed and 43 cases were obese. Baseline hormonal profile was similar in 3 groups. Total dose of administered FSH were similar in 3 groups. Number of retrieved oocytes was statistically significant higher in patients with BMI>30 but the number of mature oocytes and number of embryos were statistically lower in this group. Size of follicles showed no statistically significant difference in 3 groups. Clinical pregnancy rate was statistically significant lower in patients with BMI>30 kg/m2 and age>35 years old.

Conclusions: BMI>30 and age >35 years old has a statistically significant negative impact on IVF success rate.

Keywords: body weight index; in-vitro fertilization; outcome

Introduction

Ovulatory dysfunction is seen in about 6% of women with infertility [1]. In about 70% of cases, polycystic ovary syndrome (PCOS) is the main cause of ovulation failure [2]. PCOS is the most common hormonal disorder in women of reproductive age [3] with a prevalence of 6-10% which leads to hypergonadism, anovulation, and increased level of luteinizing hormone (LH), increased risk of early abortion, diabetes, hyperlipidemia, hypertension /cardiovascular disease, and obesity (4-5). Up to 65% of women with PCOS are overweighed or obese [6] and a body mass index (BMI) ≥30 kg/m2 is seen in >50% of cases [7].

In-vitro fertilization (IVF) is a common therapeutic modality used in infertile women. IVF has different success rates in different subgroups of patients and it is necessary to alter the common standard protocols to overcome the potential obstacles in some populations of patients and achieve the best results [8]. Although according to some studies, obesity per se or as a part of PCOS status of patient may decrease the fertilization rate and clinical pregnancy chance after IVF (probably by decreasing the oocyte count and increasing the gonadotropin resistance) but the results of different studies are still conflicting [9].

This study was conducted to evaluate the impact of pre-gestational maternal age and body weight on the outcome of IVF in women with PCOS.

Materials and Methods

Study design and setting

This retrospective study was conducted in a tertiary level referral teaching hospital with annual censuses of about 40,000. We enrolled cases from November 2016 to April 2018 conveniently. Institutional ethics committee approved our study (Code: IR.SBMU.MSP.REC.1398.070). The study was carried out in accordance with the Declaration of Helsinki (1989). Informed written consent was obtained from all patients.

Participants

All <40 years old women with PCOS who were attended in our institutional fertility clinic were eligible to participate in study. We

excluded women with BMI<18, history of previous systemic disease (diabetes mellitus, collagen-vascular diseases, hypo/hyperthyroidism, psychotic diseases, substance abuse); women whose partner had known asospermia and women who were candidate of receiving egg donation. In our clinic, there is a separate division for POCS patients. We included our cases from this division which is supervised by perinatologists.

Study Protocol

Diagnosis of PCOS was made according to the Rotterdam criteria: presence of anovulation/oligo-ovulation, signs of high androgen level (especially hirsutism), presence of polycystic ovary and/or increased ovarian size. PCOS was diagnosed when 2 of these 3 criteria were documented in patient and other conditions causing high testosterone level (like exogenous androgen administration, hyperprolactinemia, thyroid disorders, etc.) were excluded [12-13].

After including in study, demographic characteristics, weight, height, duration of infertility, duration of ovulation induction, total administered dose of FSH, IVF cycle parameters (number of retrieved and mature oocytes, mean size of follicles, number of embryos), rate of ovarian hyper-stimulation syndrome (OHSS) and clinical pregnancy rate were also derived and documented.

IVF success was defined as positive fetal heart rate in ultrasound scan 3-4 weeks after IVF. BMI was calculated as weight (kg)/height (m) ^{2}. WHO standard classification of BMI was used for patient categorization: BMI of 18.5–24.9 kg/m2 was considered "normal", BMI of 25–29.9 kg/m2 was considered as "overweight" and a BMI≥ 30 kg/m2 was considered "obese" [14].

Data Analysis

We used following formula to calculate the sample size of our study by considering the power of 90% and confidence interval of 95% with this hypothesis that the BMI impacts the outcome of IVF cycles in women with PCOS. Sample size was calculated as 176 but we included 200 cases to increase the strength of our results.

$$N = \frac{2 \times (Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}) \times \rho(1-\rho)}{(P_1 - P_2)^2}$$

Descriptive data were reported as mean (±standard deviation), maximum and minimum. Categorical data were presented with percentages. Student's t-test and Chi-Square test were used to compare the means. All analyses were done by SPSS statistical software SPSS, version 18 (SPSS, Inc., Chicago, IL).

Results

200 cases were included and analyzed. Mean BMI of studied cases was 26.88(±6.55) with a minimum of 18 and maximum of 40.6. 72 patients had normal BMI (18.5-24.9), 85 cases were overweighed (BMI=25-30) and 43 cases were obese (BMI>30). Mean duration of infertility was 5.2 (±2.1) years in studied patients with a minimum of 2 and maximum of 15 years.

IVF parameters- Duration of ovulation induction was statistically significant shorter in patients with normal BMI (P value=0.02). Number of retrieved oocytes was statistically significant higher in patients with BMI>30 but the number of mature oocytes and number of embryos were statistically lower in this group (table 2). Total dose of administered FSH, mean size of follicles and day of transfer were slimier in 3 studied groups (table 1).

Variable	Minimum	Maximum	Mean (SD)
Maternal age, years	20	40	32.5 (5.2)
BMI(kg/m2)	18	40.6	26.88(4.3)
LH(IU/L)	1	15	5.63(0.34)
FSH(IU/L)	0	12	5.90(0.18)
E2(pg./ml)	10	250	70.55(4.2)
AMH (ng /ml)	3	13	8.45(0.14)
Age of partner, years	24	57	37.39(6.3)
Number of sperms	30	150	59.14(±30.7)
Motility of sperms	30	100	99.07(±6.8)
Ante grade sperm movement	0	87	61.43(±22.5)

Abbreviations-BMI: body mass index, FSH: follicle-stimulating hormone, LH: luteinizing hormone, E2:stradiol hormone, AMH: Anti-mullerian hormone

Table1: *Baseline data*

IVF success rate- IVF was successful in 134 (67%) of cases. From 66 IVF failure cases, in 46(69.69%) cases beta-HCG was negative and in 20(30.30%) cases beta-HCG was positive but no fetal heart rate was detected in ultrasound scan. BMI had a statistically significant relationship with IVF success. Clinical pregnancy rate in obese patients was less than half of patients with normal or overweight BMI (p value=0.01). There was also a statistically significant relationship between age and IVF success (p value=0.034). success rate was about 43% in patients younger than 35 years old and about 16% in patients older than 35 years old (table 2).

Parameter	BMI, kg/m2			
	18.5-24.9 (Normal)(n=72)	25-30 (Overweight) (n=85)	>30 (Obese) (n=43)	P value
Endometrial thickness, mean(SD)	7.13	7.97	8.09	0.02*
Duration of ovulation induction, days, mean(SD)	9.80(1.72)	10.16(2.06)	10.50(1.12)	0.02*
Total dose of administered FSH, IU/L, mean(SD)	2165.21(1257.85)	2408.9(1357.54)	2632.9(1336.53)	0.72*

Number of retrieved oocytes, mean(SD)		21.73(11.85)	20.60(9.18)	23.72(11.72)	0.01*
Number of mature oocytes, mean(SD)		18.40(17.63)	16.57(9.72)	16.40(5.22)	0.01*
Mean size of follicles, mm, mean(SD)		16.69(2.25)	16.67(2.03)	16.23(1.72)	0.11*
Number of embryos, mean(SD)		10.06(4.03)	9.91(4.12)	8.97(4.56)	0.00*
OHSS occurrence, NO (%)		11(15.9%)	24(31%)	9(19.1%)	0.34†
Day of transfer, NO (%)	D2	1(1.44)	2(2.44)	1(2.17)	0.86†
	D3	5(7.24)	9(10.74)	8(14.92)	0.92†
	D4	52(75.48)	56(66.77)	29(61.72)	0.06†
	D5	11(15.96)	17(20.28)	10(21.33)	0.53†
Clinical pregnancy, NO (%)		45(62.50)	69(81.17)	20(46.51)	0.01†

**Student's t-test, †Chi-square test*

Table2: *IVF parameters and result in patients with different BMI*

Effects of age- 133 women of 200 studied PCOS cases were younger than 35 years old. From these 133 cases, in 86(64.66%) IVF outcome was positive. 67 of 200 studied women were ≥35 years old. In 32 (48.5%) of these patients IVF outcome was positive. Positive IVF outcome was statistically significant higher in <35 years old patients (table 3) (Figure 1).

		Age <35 years old (n=133)	**Age >35 years old (n=67)**	**P value**
Duration of ovulation induction, days, mean(SD)		10.13(2.0)	10.21(1.3)	0.11*
Total dose of administered FSH (IU/L), mean(SD)		2182.8(1164.8)	2772.7(1534.9)	0.06*
Number of retrieved oocytes, mean(SD)		18.46(12.2)	17.19(7.2)	0.06*
Number of mature oocytes, mean(SD)		15.77(14.7)	13.92(4.3)	0.05*
Mean size of follicles, mm, mean(SD)		16.58(2.0)	16.56(2.0)	0.48*
Number of embryos, mean(SD)		9.41(3.4)	10.04(4.9)	0.10
OHSS occurrence, NO (%)		36(29.1%)	10 (15.2%)	0.06†
Day of transfer, NO (%)	D2	4(3)	0	0.15†
	D3	13(9.7)	8(12.1)	0.85†
	D4	97(72.4)	40(60.6)	0.07†
	D5	20(14.9)1	18(27.3)	0.87†
Clinical pregnancy, NO (%)		86(64.2)	32(48.5)	0.03†

**Student's t-test, †Chi-square test*

Table3: *IVF parameters and result in patients under and above 35 years old*

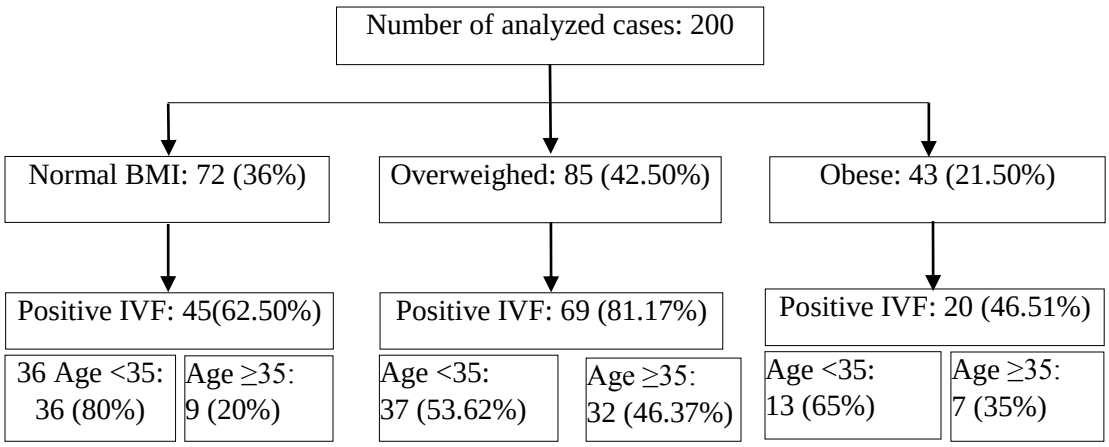

Figure1: *Summary of Results*

Discussion:

Our study evaluated the role of BMI and age in the IVF success rate in known cases of PCOS and showed that increased maternal BMI to >30 decreases the chance of clinical pregnancy especially when the maternal age is ≥35 years old.

IVF success was statistically significant lower in women with BMI>30 than the women in 2 groups of normal and overweight BMI and the difference rate was not statistically significant between normal and overweighed women. This finding is against the results of some other studies which have shown that overweighed women may has decreased chance of pregnancy due to their increased body weight. A meta-analysis on 16 studies showed that increased maternal body weight to a BMI ≥25 can increase the miscarriage rate after both spontaneous and assisted conception (10). Another systematic review on 33 studies and 47967 IVF cycles outcome showed also that BMI≥25 had significantly negative impact on the clinical pregnancy and live birth rate after IVF [11].

Subramanian et al showed also in a systematic review on 49 studies that overweight and obese women (BMI≥ 25) have lower live birth rate after assisted fertilization in comparison with women with normal body weight. This systematic review has also shown that miscarriage rate is significantly higher in women with a BMI ≥ 30 [12].

Some other studies have shown that maternal body weight has no significant effect on the outcome of assisted fertilization [13, 14]. For example, Friedler et al evaluated the effect of BMI on the live birth rate following IVF in 1654 cycles and showed that clinical pregnancy rate was similar in studied patients with BMI <25, 25-30, 30-35 and >35. Hormonal profile and response, mean number of retrieved and fertilized oocytes and number of embryos transferred were also similar in patients with different body weights in this study [15]. In another study, effects of extreme BMIs on assisted fertilization outcome was evaluated on 8145 cases and it was shown that patients with BMI>36 or <19 were the only group of studied cases with decreased chance of clinical pregnancy and live birth [16].

There are several studies on the effect of PCOS and/or obesity on the IVF cycle parameters. For example, a systematic review on 1596 articles from 1950 to 2010 showed that the number of retrieved oocytes during IVF cycles is typically higher in women with PCOS but different extra-ovarian factors our (endocrine and metabolic dysfunctions like decreased FSH and increased LH/estradiol level, hyperinsulinemia, etc.) And intra-ovarian abnormalities (abnormal level and function of follicle fluid factors and intra-follicular fluid microenvironment) impair the maturation, fertilization and implantation process in oocytes retrieved from PCOS women leading to decreased clinical pregnancy and live birth and increased miscarriage rate [17].

Evaluation of IVF cycle parameters in our PCOS patients showed that the number of retrieved oocytes was higher in patients with BMI>30 but the number of mature oocytes and number of embryos were statistically lower in this group. Although most available studies show the increased number of retrieved oocytes in PCOS patients in comparison with non-PCOS [18-19] but there are also other studies reporting the reduced number of oocytes retrieved from PCOS women during IVF cycles (20) (probably due to the effects of obesity in these women) **[**21-22**].**

Age-related results of our study showed that the IVF cycle parameters were similar in patients aged <35 and ≥35 years old but positive IVF outcome was statistically significant higher in patients younger than 35 years old. This finding is compatible with the results of Kalem M et al who showed that only the number of embryos transferred were higher in patients ≥35 years old than the younger ones [23] but the clinical pregnancy rate was higher in patients <35 and the other studies which demonstrate the independent role of age in decreasing the chance of pregnancy after assisted fertilization **[**24-25**].**

Limitations

Our study is a retrospective study with small sample size. Other multi-center prospective studies are needed to determine the exact role of maternal body weight on the IVF success. In our study, IVF outcome was defined as "clinical pregnancy" but studies focusing on live birth rate per each IVF cycle may be more beneficial for health sector policy makers to evaluate the cost-effectiveness of infertility treatments more precisely and improve the therapeutic procedures to decrease the overall perinatal complications and increase the live birth rate.

Conclusion

BMI>30 and age >35 years old has a statistically significant negative impact on IVF success rate in women with poly cystic ovary syndrome.

Statement of Ethics

Institutional ethics committee approved our study (Code: IR.SBMU.MSP.REC.1398.070). The study was carried out in accordance with the Declaration of Helsinki (1989). Informed written consent was obtained from all patients.

Conflict of Interest

The authors declare no conflicts of interest.

Funding Source

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Author Contributions:

Shahrzad Zademodares: Study design, Masoumeh Abbaspour: Case enrollment, Maryam Anbarluei: Case enrollment, Nayereh Rahmati: Case enrollment, Marzieh Fathi: Data analysis and manuscript preparation, Zahra Naeiji: Study design, Data analysis and manuscript preparation.

References

1. Yan Sheng, Guangxiu Lu, Jiayin Liu, Xiaoyan Liang, Yanping Ma, Xuehong Zhang et al. Effect of body mass index on the outcomes of controlled ovarian hyperstimulation in Chinese women with polycystic ovary syndrome: a multicenter, prospective, observational study. J Assist Reprod Genet. 2017; 34(1): 61–70.
2. Kudsy M, Alhalabi M, Al-Quobaili F. Follicular fluid Vascular Endothelial Growth Factor (VEGF) could be a predictor for pregnancy outcome in normo-responders and polycystic ovary syndrome women undergoing IVF/ICSI treatment cycles. Middle East Fertil Soc J. 2016; 21:52–56.
3. Goodman NF, Cobin RH, Futterweit W, Glueck JS, Legro RS, Carmina E. American Association of Clinical Endocrinologists (AACE); American College of Endocrinology (ACE); Androgen Excess and PCOS Society.disease state clinical review: Guide to the best practices in the evaluation and treatment of pllycystic ovary syndrpme-Part2. Endocr Pract. 2015; 21(12):1415-1426.
4. Sheehan MT. Polycystic ovarian syndrome: diagnosis and management.Clin Med Res. 2004; 2(1):13-27.
5. Barber TM, McCarthy MI, Franks S, Wass JA. Metabolic syndrome in polycystic ovary syndrome.Endokrynol Pol. 2007; 58(1):34-41.
6. Al-Azemi M, Omu FE, Omu AE. The effect of obesity on the outcome of infertility management in women with polycystic ovary syndrome.Arch Gynecol Obstet. 2004; 270(4):205-210.
7. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet 2007; 370:685-697.

8. Jungheim E, Moley K, Odem R, Chang A, Lanzendorf S, Ratts V. PCOS, obesity, and IVF. Fertility and Sterility. 2007; 88(1):S63–S64.
9. Fedorcsák P, Dale PO, Storeng R, Tanbo T, Abyholm T.The impact of obesity and insulin resistance on the outcome of IVF or ICSI in women with polycystic ovarian syndrome. Hum Reprod. 2001 Jun; 16(6):1086-1091.
10. Bani Mohammad M, Majdi A.Polycystic Ovary Syndrome (PCOS), Diagnostic Criteria, and AMH. Asian Pac J Cancer Prev. 2017; 18(1): 17–21.
11. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group 2004 Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod, 19:41–47.
12. Supramaniam P, Mittal M, McVeigh E,Nai Lim L.The correlation between raised body mass index and assisted reproductive treatment outcomes: a systematic review and meta-analysis of the evidence. Reprod Health. 2018; 15: 34.
13. Metwally M, Ong KJ, Ledger WL, Li TC. Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception? A meta-analysis of the evidence. Fertil Steril. 2008;90(3):714-726.
14. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-439.
15. Friedler S, Cohen O, Liberty G, Saar-Ryss B, Meltzer S, Lazer T. Should high BMI be a reason for IVF treatment denial? Gynecol Endocrinol. 2017 Nov; 33(11):853-856.
16. Thum MY, El-Sheikhah A, Faris R, Parikh J, Wren M, Ogunyemi T et al. The influence of body mass index to in-vitro fertilisation treatment outcome, risk of miscarriage and pregnancy outcome. J Obstet Gynaecol. 2007; 27(7):699-702.
17. Qiao J, Feng HL.Extra- and intra-ovarian factors in polycystic ovary syndrome: impact on oocyte maturation and embryo developmental competence. Hum Reprod Update. 2011; 17(1):17-33.
18. Boomsma CM, Fauser BC, Macklon NS. Pregnancy complications in women with polycystic ovary syndrome.Semin Reprod Med. 2008; 26(1):72-84.
19. Mulders AG, Laven JS, Imani B, Eijkemans MJ, Fauser BC. IVF outcome in anovulatory infertility (WHO group 2)--including polycystic ovary syndrome--following previous unsuccessful ovulation induction. Reprod Biomed Online. 2003; 7(1):50-58.
20. Robker RL.Evidence that obesity alters the quality of oocytes and embryos.Pathophysiology. 2008; 15(2):115-121.
21. Zhang JJ, Feret M, Chang L, Yang M, Merhi Z.Obesity adversely impacts the number and maturity of oocytes in conventional IVF not in minimal stimulation IVF. Gynecol Endocrinol. 2015; 31(5):409-413.
22. Metwally M, Cutting R, Tipton A, Skull J, Ledger WL, Li TC.Effect of increased body mass index on oocyte and embryo quality in IVF patients. Reprod Biomed Online. 2007;15(5):532-538.
23. Kalem M, Kalem Z, Sari, T, Ates C, Gurgan T. Effect of body mass index and age on in vitro fertilization in polycystic ovary syndrome. J Turk Ger Gynecol Assoc. 2016;17(2):83–90.
24. Harton GL, Munne S, Surrey M, Grifo J, Kaplan B, McCulloh DH, et al. Diminished effect of maternal age on implantation after preimplantation genetic diagnosis with array comparative genomic hybridization. Fertil Steril. 2013; 100:1695–1703.
25. Yan J, Wu K, Tang R, Ding L, Chen ZJ. Effect of maternal age on the outcomes of in vitro fertilization and embryo transfer (IVF-ET). Sci China Life Sci. 2012; 55(8):694-698.

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